

US009340614B2

# (12) United States Patent

Zeller et al.

# (54) ANTAGONIST ANTIBODIES DIRECTED AGAINST CALCITONIN GENE-RELATED PEPTIDE AND METHODS USING SAME

(71) Applicant: Labrys Biologics, Inc., Redwood City, CA (US)

(72) Inventors: **Joerg Zeller**, Ann Arbor, MI (US);

Kristian T. Poulsen, San Francisco, CA (US); Yasmina Noubia Abdiche, Mountain View, CA (US); Jaume Pons, San Bruno, CA (US); Sierra Jones Collier, Menlo Park, CA (US); Arnon Rosenthal, Woodside, CA (US)

(73) Assignee: LABRYS BIOLOGICS, INC.,

Redwood City, CA (US)

(\*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35

U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

Claime.

(21) Appl. No.: 14/841,479(22) Filed: Aug. 31, 2015

(65) Prior Publication Data

US 2015/0361173 A1 Dec. 17, 2015 **Related U.S. Application Data** 

- Continuation of application No. 14/719,015, filed on May 21, 2015, which is a continuation of application No. 14/251,925, filed on Apr. 14, 2014, now Pat. No. 9,115,194, which is a continuation of application No. 14/086,816, filed on Nov. 21, 2013, now Pat. No. 8,734,802, which is a continuation of application No. 13/870,871, filed on Apr. 25, 2013, now Pat. No. 8,597,649, which is a continuation of application No. 13/179,846, filed on Jul. 11, 2011, now Pat. No. 8,586,045, which is a division of application No. 12/093,638, filed as application PCT/IB2006/003181 on Nov. 2, 2006, now Pat. No. 8,007,794.
- (60) Provisional application No. 60/736,623, filed on Nov. 14, 2005.
- (51) Int. Cl.

11100 010	
A61K 39/395	(2006.01)
C12P 21/08	(2006.01)
C07K 16/00	(2006.01)
C07K 16/26	(2006.01)
C07K 16/18	(2006.01)
A61K 31/4045	(2006.01)
A61K 39/00	(2006.01)

(52) **U.S. Cl.** 

 (10) Patent No.: US

US 9,340,614 B2

(45) **Date of Patent:** 

\*May 17, 2016

## (58) Field of Classification Search

None

See application file for complete search history.

#### (56) References Cited

#### U.S. PATENT DOCUMENTS

4,816,567 A	3/1989	Cabilly et al.
5,116,964 A	5/1992	Capon et al.
5,500,362 A	3/1996	Robinson et al.
5,545,806 A	8/1996	Lonberg et al.
5,545,807 A	8/1996	Surani et al.
5,569,825 A	10/1996	Lonberg et al.
5,625,126 A	4/1997	Lonberg et al.
5,633,425 A	5/1997	Lonberg et al.
5,661,016 A	8/1997	Lonberg et al.
5,750,373 A	5/1998	Garrard et al.
5,821,337 A	10/1998	Carter et al.
5,851,556 A	12/1998	Breton et al.
5,935,586 A	8/1999	De Lacharriere et al.
6,168,809 B1	1/2001	De Lacharriere et al.
6,180,370 B1	1/2001	Queen et al.
6,313,097 B1	11/2001	Eberlein et al.
6,344,438 B1	2/2002	De Lacharriere et al.
6,509,014 B1	1/2003	De Lacharriere et al.
6,521,609 B1	2/2003	Doods et al.

### (Continued)

#### FOREIGN PATENT DOCUMENTS

CN 1308676 A 8/2001 CN 1671711 A 9/2005

# (Continued) OTHER PUBLICATIONS

Adam, et al. Severity of mucosal inflammation as a predictor for alterations of visceral sensory function in a rat model. Pain. Jul. 2006;123(1-2):179-86. Epub Apr. 12, 2006.

Adwanikar, et al. Spinal CGRP1 receptors contribute to supraspinally organized pain behavior and pain-related sensitization of amygdala neurons. Pain. Nov. 2007;132(1-2):53-66. Epub Mar. 1, 2007.

Al-Lazikani, et al. Standard conformations for the canonical structures of immunoglobulins. J Mol Biol. Nov. 7, 1997;273(4):927-48. Almagro, et al. Antibody engineering: humanization, affinity maturation, and selection technique. Therapeutic Monoclonal Antibodies, Chapter 13, pp. 311-334, 2009.

Chapter 13, pp. 311-334, 2009.
Amara, et al. Expression in brain of a messenger RNA encoding a novel neuropeptide homologous to calcitonin gene-related peptide. Science. Sep. 13, 1985;229(4718):1094-7.

Ambalavanar, et al. Deep tissue inflammation upregulates neuropeptides and evokes nociceptive behaviors which are modulated by a neuropeptide antagonist. Pain. Jan. 2006;120(1-2):53-68. Epub Dec. 13, 2005.

American Academy of Neurology. New Drugs Offer Hope for Migraine Prevention. Apr. 22, 2014.

#### (Continued)

Primary Examiner — Christine J Saoud Assistant Examiner — Jon M Lockard

(74) Attorney, Agent, or Firm — Wilson Sonsini Goodrich & Rosati

### (57) ABSTRACT

The invention features methods for preventing or treating CGRP associated disorders such as vasomotor symptoms, including headaches (e.g., migraine, cluster headache, and tension headache) and hot flushes, by administering an anti-CGRP antagonist antibody. Antagonist antibody G1 and antibodies derived from G1 directed to CGRP are also described.

## 20 Claims, 16 Drawing Sheets